PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3 -32536A	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/06478	International filing date *(day/month/year)* 18.06.2003	Priority date *(day/month/year)* 20.06.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/08		
Applicant NOVARTIS CONSUMER HEALTH S.A.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
20.09.2003	02.08.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Sindel, U Telephone No. +49 89 2399-7064

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/06478

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-16 as originally filed

Claims, Numbers

1-17 received on 13.12.2003 with letter of 11.12.2003

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 5

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☒ the claims, or said claims Nos. 5 are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-4, 6-10, 13-14, 16
	No:	Claims	11, 12, 15, 17
Inventive step (IS)	Yes:	Claims	1-4, 6-10, 13-14, 16
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims	1-4, 6-17 (YES)

2. Citations and explanations

see separate sheet

The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: US 4 402 949
D2: US 5 876 744
D3: US 2001/0051613
D4: WO 91/12808

Item I

The amendments filed with the letter dated 11.12.2003 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT.
The amendment concerned is the subject-matter of present claim 5.
Therefore, no opinion will be formulated for the subject-matter of present claim 5 with regard to novelty, inventive step or industrial applicability.

Item V

1) Novelty

The subject matter of claims 11, 12, 15 and 17 is not regarded as new in the sense of Article 33(2) PCT.

D1 already describes a stable solution consisting essentially of the actives lidocain and dihydroergotamine, the mucopolysaccharide heparin, water and propylene glycol (see claims 1, 14 and example III). These ingredients sum up to 95,5% of the total injectable formulation, so that the solution "consists essentially" of these compounds (see example III). Excipients like preserving agents may be added (see column 4, lines 24-27). Since the solution is injectable, it fulfills also the purity requirements for nasal administration.

Hence, the subject matter of claims 11, 12, 15 and 17 is not new.

2) Inventive step

The subject matter of claims 1-4, 6-10, 13-14 and 16 seems to involve an inventive step in the sense of Article 33(3) PCT in view of the prior art.

The problem to be solved in the present application is the provision of a nasal

composition comprising actives others than fexofenadine and having good moisturizing properties.
The solution provided is a composition comprising an active, a mucopolysaccharide and propylene glycol.

D1 deals with stabilizing solutions for injection (see abstract) and does not provide any guidance to improve nasal formulations with mucopolysaccharides and propylene glycol.
D2 describes mucoadhesive compositions with polycarbophil, polyvinyl alcohol and a biopolymer, like certain mucopolysaccharides, as essential components (see abstract). In example 24, the use of 1% propylene glycol together with these components and some other excipients for a gynaecologic gel is accidentally disclosed.There is no hint given that a beneficial nasal composition could be obtained.
D3 discloses a nasal formulation of fexofenadine which overcomes the solubility problem of the active. Propylene glycol and polysaccharides are listed as possible excipients (see claims 1, 4, 10), but there is no hint given that this specific combination could lead to excellent moisturizing properties.
In **D4**, artificial tears comprising phospholipid and propylene glycol are disclosed (see claims 1, 3). Hyaluronic acid and actives like vasoconstricting agents are optional components (see claims 1, 5).

Hence, the subject matter of claims 1-4, 6-10, 13-14 and 16 involves an inventive step

3) Industrial applicability
The subject matter of claims 1-4 and 6-17 is industrially applicable in the sense of Article 33(4) PCT.

Claims

1. A nasal pharmaceutical composition which comprises
(a) at least one active substance suitable for nasal administration, which active substance is selected from the group consisting of xylometazoline, naphazoline, fenoxazoline, oxymetazoline, tetrahydrozoline, tramazoline, phenylephrine, ephedrine, epinephrine, and nasally acceptable salts of any of these compounds,
(b) a mucopolysaccharide which is selected from the group consisting of chondroitin, hyaluronic acid, dermatan, keratan, heparin, acemannan, and nasally acceptable salts of any of said compounds, and
(c) propylene glycol.

2. A composition according to claim 1, wherein the active substance (a) is xylometazoline or a nasally acceptable salt thereof.

3. A composition according to claim 1 or claim 2, wherein the mucopolysaccharide (b) is chondroitin sulfate.

4. A composition according to any one of claims 1-3, wherein propylene glycol (c) is present in an amount of from 0.5 up to 10 % (w/w) of the total composition.

5. A composition according to any one of claims 1-3, wherein propylene glycol (c) is present in an amount of from 1.5 up to 5 % (w/w) of the total composition.

6. A composition according to any one of claims 1-5, which includes water as vehicle.

7. A composition according to any one of claims 1-6, which in addition includes a nasally acceptable film-forming agent.

8. A composition according to any one of claims 1-7, which in addition includes an essential oil of a plant.

9. A composition according to any one of claims 1-8, which in addition includes a nasally acceptable preservative.

10. A composition according to any one of claims 1-8, which is devoid of an additional nasally acceptable preservative.

11. A nasal pharmaceutical composition which consists essentially of
(a) at least one active substance suitable for nasal administration,
(b) a mucopolysaccharide,
(c) propylene glycol, and
water,
with the proviso that said composition is devoid of fexofenadine and pharmaceutically acceptable salts thereof.

12. A nasal pharmaceutical composition which consists essentially of
(a) at least one active substance suitable for nasal administration,
(b) a mucopolysaccharide,
(c) propylene glycol,
a nasally acceptable preservative, and
water,
with the proviso that said composition is devoid of fexofenadine and pharmaceutically acceptable salts thereof.

13. A composition according to claim 11 or claim 12, wherein the active substance (a) is selected from the group consisting of xylometazoline, naphazoline, fenoxazoline, oxymetazoline, tetrahydrozoline, tramazoline, phenylephrine, ephedrine, epinephrine, and nasally acceptable salts of any of these compounds,

14. A composition according to claim 13, wherein the active substance (a) is xylometazoline or a nasally acceptable salt thereof.

15. A nasal pharmaceutical composition according to any one of claims 11-14, wherein the mucopolysaccharide (b) is selected from the group consisting of chondroitin, hyaluronic acid, dermatan, keratan, heparin, acemannan, and nasally acceptable salts of any of said compounds.

16. A composition according to claim 15, wherein the mucopolysaccharide (b) is chondroitin sulfate.

17. A composition according to any one of claims 1-16, which is in the form of drops, a solution, a spray or a metered-dose spray.